

**Form PTO-1449 Modified**Docket No.  
**ISIS-3013**Serial No.  
**09/403,539**List of Patent and Publications  
Cited by Applicant  
(Use several sheets if necessary)Applicant  
**Nicholas M. Dean et al.**U.S. Department of Commerce  
Patent and Trademark OfficeFiling Date  
**January 4, 2000**Group  
**Not Yet Assigned****OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

	<b>AA</b>	Agrawal et al. (eds.), "Methods of Molecular Biology", in <i>Protocols for Oligonucleotide Conjugates</i> , Agrawal, S. (ed.), Humana Press, New Jersey, 1994, Vol. 26, 1-72
	<b>AB</b>	Agrawal, S. et al., "Pharmacokinetics, biodistribution, and stability of oligodeoxynucleotide phosphorothioates in mice", <i>Proc. Natl. Acad. Sci.</i> , 1991, 88, 7595-7599
	<b>AC</b>	Albert, P.R. et al., "Antisense knockouts: molecular scalpels for the dissection of signal transduction", <i>Trends Pharmacol. Sci.</i> , 1994, 15, 250-254
	<b>AD</b>	Benet, L.Z. et al., "Pharmacokinetics: The Dynamics of Drug Absorption, Distribution, and Elimination", <i>Goodman &amp; Gilman's The Pharmacological Basis of Therapeutics</i> , 9th Ed., Hardman et al. (eds.), McGraw-Hill, New York, NY, 1996, Chapter 1, 3-9
<i>me</i>	<b>AE</b>	Berge, S.M. et al., "Pharmaceutical Salts", <i>J. Pharm. Sci.</i> , 1977, 66, 1-19
	<b>AF</b>	Block, L., "Medicated Applications", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, 1990, Ch. 87, 1596-1614
<i>me</i>	<b>AG</b>	Brunton, L.L., "Agents Affecting Gastrointestinal Water Flux and motility; Emesis and Antiemetics; Bile Acids and Pancreatic Enzymes", <i>Goodman &amp; Gilman's The Pharmacological Basis of Therapeutics</i> , 9th Ed., Hardman et al. (Eds.), McGraw-Hill, New York, 1996, Chapter 38, 934-935
<i>me</i>	<b>AH</b>	Buur, A. et al., "Penetration of 5-Fluorouracil and prodrugs across the intestine of the albino rabbit: Evidence for shift in absorption site from the upper to the lower region of the gastrointestinal tract by prodrugs", <i>J. Controlled Release</i> , 1990, 14, 43-51
<i>me</i>	<b>AI</b>	Chonn, A. et al., "Recent advances in liposomal drug-delivery systems", <i>Curr. Opin. Biotechnology</i> , 1995, 6, 698-708
	<b>AJ</b>	Crooke, S.T. et al., "Progress in the development and patenting of antisense drug discovery technology", <i>Exp. Opin. Ther. Patents</i> , 1996, 6, 855-870
	<b>AK</b>	Crooke, S.T. et al., "Pharmacokinetic Properties of Several Novel Oligonucleotide Analogs in mice", <i>J. Pharmacol. Exp. Therapeutics</i> , 1996, 277, 923-937

**EXAMINER****DATE CONSIDERED**

**Form PTO-1449 Modified**Docket No.  
**ISIS-3013**Serial No.  
**09/403,539**List of Patent and Publications  
Cited by Applicant  
(Use several sheets if necessary)Applicant  
**Nicholas M. Dean et al.**U.S. Department of Commerce  
Patent and Trademark OfficeFiling Date  
**January 4, 2000**Group  
**Not Yet Assigned****OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

	<b>AL</b>	Crooke, R.M., " <i>In Vitro and In Vivo Toxicology of First Generation Analogs</i> ," in <i>Antisense Research and Applications</i> , Crooke et al. (eds.), CRC Press, Inc., Boca Raton, FL, 1993, Chapter 27, pages 471-492
	<b>AM</b>	Dean, N.M. et al., "Inhibition of protein kinase C- $\alpha$ expression in mice after systemic administration of phosphorothioate antisense oligodeoxynucleotides", <i>Proc. Natl. Acad. Sci.</i> , 1994, 91, 11762-11766
	<b>AN</b>	DiSanto, A.R., "Bioavailability and Bioequivalency Testing", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, 1990, Ch. 76, 1451-1458
me	<b>AO</b>	El-Hariri, L.M. et al., "The Mitigating Effects of Phosphatidylcholines on Bile Salt- and Lysophosphatidylcholine-induced Membrane Damage", <i>J. Pharm. Pharmacol.</i> , 1992, 44, 651-654
	<b>AP</b>	Geary, R.S. et al., "Characterization of Ethiofos Absorption in the Rat Small Intestine", <i>Biopharmaceutics &amp; Drug Disposition</i> , 1991, 12, 261-274
	<b>AQ</b>	Gebeyehu, G. et al., "Novel bitinylated nucleotide - analogs for labeling and colorimetric detection of DNA", <i>Nucl. Acids Res.</i> , 1987, 15, 4513-4534
	<b>AR</b>	Genetic Engineering News: "ISIS Pharmaceuticals Demonstrates Efficiency in Crohn's Disease with its Antisense Drug", March 1, 1997, pg 1 and 34
me	<b>AS</b>	Harvey, S.C., "Drug Absorption, Action, and Disposition", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, 1990, Ch. 35, 711-715
me	<b>AT</b>	Hirahata, "Study of DDS to the Lymphnode-Metastases of the Gastric Cancer by the Endoscopic Injection of Lip-ADM," <i>Jpn. J. Cancer Chemother.</i> , 1992, 19(10), 1591-1594 (English summary attached)
me	<b>AU</b>	Iverson, P., " <i>In Vivo Studies with Phosphorothioate Oligonucleotides: Rationale for Systemic Therapy</i> ," in: <i>Antisense Research and Applications</i> , Crooke et al. (eds.), CRC Press, Inc., Boca Raton, FL, 1993, Chapter 26, pages 461-469
	<b>AV</b>	Iverson, P., "In Vivo studies with phosphorothioate oligonucleotides: pharmacokinetics prologue", <i>Anti-Cancer Drug Des.</i> , 1991, 6, 531-538

**EXAMINER****DATE CONSIDERED**

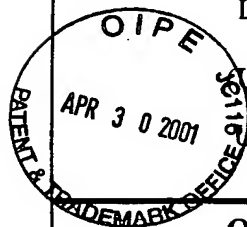
**Form PTO-1449 Modified**Docket No.  
**ISIS-3013**Serial No.  
**09/403,539**List of Patent and Publications  
Cited by Applicant  
(Use several sheets if necessary)Applicant  
**Nicholas M. Dean et al.**U.S. Department of Commerce  
Patent and Trademark OfficeFiling Date  
**January 4, 2000**Group  
**Not Yet Assigned****OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

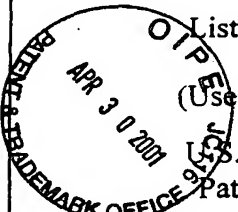


	<b>AW</b>	Kabanov, A.V., "A new class of antivirals: antisense oligonucleotides combined with a hydrophobic substituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells", <i>FEBS Letts.</i> , <b>1990</b> , 259, 327-330
	<b>AX</b>	Katocs, A.S. et al., "Biological Testing", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, <b>1990</b> , Ch. 27, 484-494
	<b>AY</b>	Kornberg, A. et al., <i>DNA Replication</i> , W.H. Freeman & Co., San Francisco, <b>1980</b> , 4-7
	<b>AZ</b>	Kornberg, A., <i>DNA Replication</i> , W.H. Freeman and Co., San Francisco, <b>1980</b> , 75-77
<i>MS</i>	<b>BA</b>	Lee, V.H.L. et al., "Mucosal Penetration Enhancers For Facilitation of Peptide and Protein Drug Absorption", <i>Crit. Rev. Ther. Drug Carrier Systems</i> , <b>1991</b> , 8, 91-192
	<b>BB</b>	Leeds, J.M. et al., "Quantitation of Phosphorothioate Oligonucleotides in Human Plasma", <i>Analyt. Biochem.</i> , <b>1996</b> , 235, 36-43
	<b>BC</b>	Letsinger, R.L. et al., "Cholesteryl-conjugated oligonucleotides: Synthesis, properties and activity as inhibitors of replication of human immunodeficiency virus in cell culture", <i>Proc. Natl. Acad. Sci.</i> <b>1989</b> , 86, 6553-6556
	<b>BD</b>	Longer, M.A. et al., "Sustained-Release Drug Delivery Systems", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, <b>1990</b> , Ch. 91, 1676-1693
	<b>BE</b>	Manoharan, M. et al., "Lipidic Nucleic Acids", <i>Tetrahedron Letts.</i> , <b>1995</b> , 36, 3651-3654
	<b>BF</b>	Manoharan M. et al., "Oligonucleotide Conjugates: Alteration of the Pharmacokinetic Properties of Antisense Agents", <i>Nucleosides and Nucleotides</i> , <b>1995</b> , 14, 969-973
	<b>BG</b>	Manoharan, M. et al., "Introduction of a Lipophilic Thioether Tether in the Minor Groove of Nucleic Acids for Antisense Applications", <i>Bioorg. Med. Chem. Letts.</i> , <b>1993</b> , 3, 2765-2770

**EXAMINER****DATE CONSIDERED**

**Form PTO-1449 Modified**Docket No.  
**ISIS-3013**Serial No.  
**09/403,539**List of Patent and Publications  
Cited by Applicant  
(Use several sheets if necessary)Applicant  
**Nicholas M. Dean et al.**U.S. Department of Commerce  
Patent and Trademark OfficeFiling Date  
**January 4, 2000**Group  
**Not Yet Assigned****OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

	<b>BH</b>	Manoharan, M. et al., "Chemical Modifications to Improve Uptake and Bioavailability of Antisense Oligonucleotides", <i>Annals NY Acad. Sciences</i> , <b>1992</b> , 660, 306-309
	<b>BI</b>	Manoharan M. et al., "Cholic Acid-Oligonucleotide Conjugates for Antisense Applications", <i>Bioorganic Med. Chem. Letts.</i> , <b>1994</b> , 4, 1053-1060
	<b>BJ</b>	Martin, P., "Ein neuer Zugang zu 2'-O-Alkylribonucleosiden und Eigenschaften deren Oligonucleotide", <i>Helvetica Chemica Acta</i> , <b>1995</b> , 78, 486-504 (English summary included)
	<b>BK</b>	Mishra, R.K. et al., "Improved leishmanicidal effect of phosphorotioate antisense oligonucleotides by LDL-medicated delivery", <i>Biochim. Et Biophysica</i> , <b>1995</b> , 1264, 229-237
	<b>BL</b>	Miyao, T. et al., "Stability and Pharmacokinetic Characteristics of Oligonucleotides Modified at Terminal Linkages in Mice", <i>Antisense Res. &amp; Dev.</i> , <b>1995</b> , 5, 115-121
<i>me</i>	<b>BM</b>	Muranishi, S., "Absorption Enhancers", <i>Crit. Rev. Ther. Drug Carrier Systems</i> , <b>1990</b> , 7, 1-33
	<b>BN</b>	Nairn, J.G., "Solutions, Emulsions, Suspensions and Extracts", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, <b>1990</b> , Ch. 83, 1519-1544
	<b>BO</b>	Nielsen, P.E. et al., "Sequence-Selective Recognition of DNA by Strand Displacement with a Thymine-Substituted Polyamide", <i>Science</i> , <b>1991</b> , 254, 1497-1500
	<b>BP</b>	Nies, A.S. et al., "Principles of Therapeutics", <i>Goodman &amp; Gilman's The Pharmacological Basis of Therapeutics</i> , 9th Ed., Hardman et al. (eds.), McGraw-Hill, New York, NY, <b>1996</b> , Ch. 3, 43-62
	<b>BQ</b>	Oberhauser, B. et al., "Effective incorporation of 2'-O-methyl-oligonucleotides into liposomes and enhanced cell association through modification with thiocholesterol", <i>Nucl. Acids Res.</i> , <b>1992</b> , 20, 533-538
	<b>BR</b>	Porter, S.C., "Coating of Pharmaceutical Dosage Forms", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, <b>1990</b> , Ch. 90, 1666-1675

**EXAMINER****DATE CONSIDERED**

<b>Form PTO-1449 Modified</b>   List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office		Docket No. <b>ISIS-3013</b>	Serial No. <b>09/403,539</b>
		Applicant <b>Nicholas M. Dean et al.</b>	
		Filing Date <b>January 4, 2000</b>	Group <b>Not Yet Assigned</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
	<b>BS</b>	Robertson, D., "Chrohn's trial shows the pros of antisense", <i>Nature Biotech.</i> , 1997, 15, 209	
	<b>BT</b>	Rudnic, E. et al., "Oral Solid Dosage Forms", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, 1990, Ch. 89, 1633-1665	
	<b>BU</b>	Saison-Behmoaras, T. et al., "Short modified antisense oligonucleotides directed against Ha-ras point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation", <i>EMBO J.</i> , 1991, 10, 1111-1118	
	<b>BV</b>	Shea, R.G. et al., "Synthesis, hybridization properties and antiviral activity of lipid-oligodeoxynucleotide conjugates", <i>Nucl. Acids Res.</i> , 1990, 18, 3777-3783	
	<b>BW</b>	Svinarchuk, F.P. et al., "Inhibition of HIV proliferation in MT-4 cells by antisense oligonucleotide conjugated to lipophilic groups", <i>Biochimie</i> , 1993, 79, 49-54	
	<b>BX</b>	Takahashi, H. et al., "The Use of a Perfluorochemical Emulsion as a Bascular Perfusate in Drug Absorption", <i>J. Pharm. Pharmacol.</i> , 1988, 40, 252-257	
	<b>BY</b>	Takakura, Y. et al., "Uptake Characteristics of Oligonucleotides in the Isolated Rat Liver Perfusion System", <i>Antisense &amp; Nuc. Acid Drug Dev.</i> , 1996, 6, 177-183	
	<b>BZ</b>	van Berge-Henegouwen, G.P., "Pharmacology of Chenodeoxycholic Acid", <i>Gastroenterology</i> , 1977, 73, 300-309	
	<b>CA</b>	Vasseur, J.J. et al., "Oligonucleosides: Synthesis of a Novel Methylhydroxylamine-linked Nucleoside Dimer and Its Incorporation into Antisense Sequences", <i>J. Am. Chem. Soc.</i> , 1992, 114, 4006-4007	
	<b>CB</b>	Wahlestedt, C. et al., "Antisense oligodeoxynucleotides to NMDA-R1 receptor channel protect cortical neurons from excitotoxicity and reduce focal ischaemic infarctions", <i>Nature</i> , 1993, 363, 260-263	
	<b>CC</b>	Wahlestedt, C. et al., "Modulation of Anxiety and Neuropeptide Y-Y1 Receptors by Antisense Oligodeoxynucleotides", <i>Science</i> , 1993, 259, 528-531	
	<b>CD</b>	Yamashita, S. et al., "Effects of diclofenac sodium and disodium ethylenediaminetetraacetate on electrical parameters of the mucosal membrane and their relation to the permeability enhancing effects in the rat jejunum", <i>J. Pharm. Pharmacol.</i> , 1987, 39, 621-626	
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>	

**Form PTO-1449 Modified**Docket No.  
**ISIS-3013**Serial No.  
**09/403,539**List of Patent and Publications  
Cited by Applicant

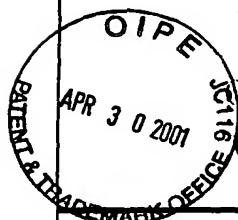
(Use several sheets if necessary)

U.S. Department of Commerce  
Patent and Trademark OfficeApplicant  
**Nicholas M. Dean et al.**Filing Date  
**January 4, 2000**Group  
**Not Yet Assigned****U. S. PATENT DOCUMENTS**

Examiner Initial		Document No.	Date	Name	Class	Subclass
	CE	4,309,404	01/05/82	DeNeale et al.	424	21
	CF	4,309,406	01/05/82	Guley et al.	424	21
	CG	4,426,330	01/17/84	Sears	260	403
	CH	4,534,899	08/13/85	Sears	260	403
	CI	4,556,552	12/03/85	Porter et al.	424	32
	CJ	4,689,320	08/25/87	Kaji	514	44
	CK	4,704,295	11/03/87	Porter et al.	427	3
	CL	4,806,463	02/21/89	Goodchild et al.	435	5
	CM	4,835,263	05/30/89	Nguyen et al.	536	27
	CN	5,004,810	04/02/91	Draper	536	27

**FOREIGN PATENT DOCUMENTS**

Examiner Initial		Document No.	Date	Country	Translation	
					YES	NO
	CO	WO 92/20823	11/26/92	PCT	X	
	CP	WO 93/24510	12/09/93	PCT	X	
	CQ	WO 94/26764	11/24/94	PCT	X	
	CR	WO 96/20732	07/11/96	PCT	X	
	CS	WO 96/32496	10/17/96	PCT	X	
	CT	WO 96/34008	10/31/96	PCT	X	
	CU	WO 97/05267	02/13/97	PCT	X	

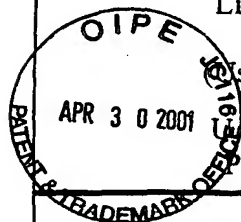
**EXAMINER****DATE CONSIDERED**

**Form PTO-1449 Modified**Docket No.  
**ISIS-3013**Serial No.  
**09/403,539**List of Patent and Publications  
Cited by Applicant

(Use several sheets if necessary)

Applicant  
**Nich. las M. Dean et al.**Filing Date  
**January 4, 2000**Group  
**Not Yet Assigned**U.S. Department of Commerce  
Patent and Trademark Office**U. S. PATENT DOCUMENTS**

Examiner Initial		Document No.	Date	Name	Class	Subclass
	CV	5,013,556	05/07/91	Woodle et al.	424	450
	CW	5,034,506	07/23/91	Summerton et al.	528	391
	CX	5,087,617	02/11/92	Smith	514	44
	CY	5,098,890	03/24/92	Gerwirtz et al.	514	44
	CZ	5,108,921	04/28/92	Low et al.	435	240.1
	DA	5,135,917	08/04/92	Burch	514	44
	DB	5,138,045	08/11/92	Cook et al.	536	27
	DC	5,166,195	11/24/92	Ecker	514	44
	DD	5,194,428	03/16/93	Agrawal et al.	514	44
	DE	5,212,295	05/18/93	Cook	536	26.7
	DF	5,213,804	05/25/93	Martin et al.	424	450
	DG	5,218,105	06/08/93	Cook et al.	536	25.31
	DH	5,227,170	07/13/93	Sullivan	424	450
	DI	5,242,906	09/07/93	Pagano et al.	514	44
	DJ	5,264,221	11/23/93	Tagawa et al.	424	450
	DK	5,264,423	11/23/93	Cohen et al.	514	44
	DL	5,276,019	01/04/94	Cohen et al.	514	44
	DM	5,286,717	02/15/94	Cohen et al.	514	44
	DN	5,354,844	10/11/94	Beug et al.	530	345
	DO	5,356,633	10/18/94	Woodle et al.	424	450
<b>EXAMINER</b>				<b>DATE CONSIDERED</b>		



**Form PTO-1449 Modified**Docket No.  
**ISIS-3013**Serial No.  
**09/403,539****RECEIVED**List of Patent and Publications  
Cited by Applicant  
(Use several sheets if necessary)Applicant  
**Nicholas M. Dean et al.**

MAY 02 2001

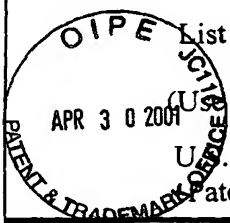
TECH CENTER 1800/290

U.S. Department of Commerce  
Patent and Trademark OfficeFiling Date  
**January 4, 2000**Group  
**Not Yet Assigned****U. S. PATENT DOCUMENTS**

Examiner Initial		Document No.	Date	Name	Class	Subclass
	DP	5,378,825	01/03/95	Cook et al.	536	25.34
	DQ	5,386,023	01/31/95	Sanghvi et al.	536	25.3
	DR	5,395,619	03/07/95	Zalipsky et al.	424	450
	DS	5,416,016	05/16/95	Low et al.	435	240.1
	DT	5,417,978	05/23/95	Tari et al.	424	450
	DU	5,457,191	10/10/95	Cook et al.	536	27.13
	DV	5,459,127	10/17/95	Felgner et al.	514	7
	DW	5,459,255	10/17/95	Cook et al.	536	27.13
	DX	5,462,854	10/31/95	Coassin et al.	435	6
	DY	5,469,854	11/28/95	Unger et al.	128	662.02
	DZ	5,506,351	04/09/96	McGee	536	55.3
	EA	5,512,295	04/30/96	Kornberg et al.	424	450
	EB	5,521,291	05/28/96	Curiel et al.	530	391.7
	EC	5,521,302	05/28/96	Cook	536	25.31
	ED	5,527,528	06/18/96	Allen et al.	424	178.1
	EE	5,534,259	06/09/96	Zalipsky et al.	424	450
	EF	5,534,496	07/09/96	Lee et al.	514	17
	EG	5,539,082	07/23/96	Nielsen et al.	530	300
	EH	5,541,307	07/30/96	Cook et al.	536	23.1
	EI	5,543,152	08/06/96	Webb et al.	424	450
<b>EXAMINER</b>				<b>DATE CONSIDERED</b>		





<b>Form PTO-1449 Modified</b>   List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office				Docket No. <b>ISIS-3013</b>		Serial No. <b>09/403,539</b>	
				Applicant <b>Nicholas M. Dean et al.</b>			
				Filing Date <b>January 4, 2000</b>		Group <b>Not Yet Assigned</b>	
<b>U. S. PATENT DOCUMENTS</b>							
Examiner Initial		Document No.	Date	Name	Class	Subclass	
	EJ	5,543,158	08/06/96	Gref et al.	424	501	
	EK	5,547,932	08/20/96	Curiel et al.	435	65	
	EL	5,554,746	09/10/96	Ravikumar et al.	540	200	
	EM	5,556,948	09/17/96	Tagawa et al.	530	391.9	
	EN	5,571,902	11/05/96	Ravikumar et al.	536	22.1	
	EO	5,578,718	11/26/96	Cook et al.	536	27.21	
	EP	5,580,575	12/03/96	Unger et al.	424	450	
	EQ	5,583,020	12/10/96	Sullivan	435	172.3	
	ER	5,587,361	12/24/96	Cook et al.	514	44	
	ES	5,587,469	12/24/96	Cook et al.	536	23.1	
	ET	5,587,470	12/24/96	Cook et al.	536	23.1	
	EU	5,591,721	01/07/97	Agrawal et al.	514	44	
	EV	5,595,756	01/21/97	Bally et al.	424	450	
	EW	5,595,978	01/21/97	Draper et al.	514	44	
	EX	5,599,797	02/04/97	Cook et al.	514	44	
<b>EXAMINER</b>				<b>DATE CONSIDERED</b>			